

CLAIMS

1. A non-naturally occurring nucleic acid molecule which encodes wild-type human p53 protein as shown in SEQ ID NO: 54-57, wherein said nucleic acid employs a plurality of alternative codons to those present in naturally occurring wild-type human p53 coding sequence as shown in SEQ ID NO: 58-61, wherein at least a portion of said alternative codons provide additional unique restriction sites to the human p53 coding sequence.
2. The nucleic acid molecule of claim 1 wherein at least a portion of said alternative codons are more preferred for usage in mammalian cells.
3. The nucleic acid molecule of claim 1 wherein at least a portion of said alternative codons are more preferred for usage in yeast cells.
4. The nucleic acid molecule of claim 1 wherein at least a portion of said alternative codons are more preferred for usage in bacterial cells.
5. The nucleic acid molecule of claim 1 wherein at least 5 alternative codons are employed.
6. The nucleic acid molecule of claim 1 wherein at least 10 alternative codons are employed.
7. The nucleic acid molecule of claim 1 wherein at least 15 alternative codons are employed.
8. The nucleic acid molecule of claim 1 wherein at least 20 alternative codons are employed.
9. The nucleic acid molecule of claim 1 wherein at least 25 alternative codons are employed.
10. The nucleic acid molecule of claim 1 wherein at least 30 alternative codons are employed.
11. The nucleic acid molecule of claim 1 wherein at least 50 alternative codons are employed.
12. The nucleic acid molecule of claim 1 wherein at least 75 alternative codons are employed.
13. The nucleic acid molecule of claim 1 wherein at least 100 alternative codons are employed.

14. The nucleic acid molecule of claim 1 wherein at least 120 alternative codons are employed.

15. The nucleic acid molecule of claim 1 wherein at least 5 additional restriction sites are provided.

16. The nucleic acid molecule of claim 1 wherein at least 10 additional restriction sites are provided.

17. The nucleic acid molecule of claim 1 wherein at least 15 additional restriction sites are provided.

18. The nucleic acid molecule of claim 1 wherein at least 20 additional restriction sites are provided.

19. The nucleic acid molecule of claim 1 wherein at least 25 additional restriction sites are provided.

20. The nucleic acid molecule of claim 1 wherein at least 30 additional restriction sites are provided.

21. The nucleic acid molecule of claim 1 which has the nucleotide sequence shown in SEQ ID NO: 1, 62, 63, or 64.

22. The nucleic acid molecule of claim 1 which has the nucleotide sequence shown in SEQ ID NO: 2, 65, 66, or 67.

23. The nucleic acid molecule of claim 1 which has the nucleotide sequence shown in SEQ ID NO: 3, 68, 69, or 70.

24. A non-naturally occurring nucleic acid molecule which employs a plurality of alternative codons to those present in naturally occurring wild-type human p53 coding sequence, said alternative codons causing no amino acid changes from wild-type human p53, wherein at least a portion of said alternative codons provide additional unique restriction sites to the human p53 coding sequence, said nucleic acid further comprising a p53 mutation found in a human cancer.

25. The nucleic acid molecule of claim 24 wherein at least a portion of said alternative codons are more preferred for usage in mammalian cells.

26. The nucleic acid molecule of claim 24 wherein at least a portion of said alternative codons are more preferred for usage in yeast cells.

27. The nucleic acid molecule of claim 24 wherein at least a portion of said alternative codons are more preferred for usage in bacterial cells.

28. The nucleic acid molecule of claim 24 wherein at least 5 alternative codons are employed.

29. The nucleic acid molecule of claim 24 wherein at least 10 alternative codons are employed.

30. The nucleic acid molecule of claim 24 wherein at least 15 alternative codons are employed.

31. The nucleic acid molecule of claim 24 wherein at least 20 alternative codons are employed.

32. The nucleic acid molecule of claim 24 wherein at least 25 alternative codons are employed.

33. The nucleic acid molecule of claim 24 wherein at least 30 alternative codons are employed.

34. The nucleic acid molecule of claim 24 wherein at least 50 alternative codons are employed.

35. The nucleic acid molecule of claim 24 wherein at least 75 alternative codons are employed.

36. The nucleic acid molecule of claim 24 wherein at least 100 alternative codons are employed.

37. The nucleic acid molecule of claim 24 wherein at least 120 alternative codons are employed.

38. The nucleic acid molecule of claim 24 wherein at least 5 additional restriction sites are provided.

39. The nucleic acid molecule of claim 24 wherein at least 10 additional restriction sites are provided.

40. The nucleic acid molecule of claim 24 wherein at least 15 additional restriction sites are provided.

41. The nucleic acid molecule of claim 24 wherein at least 20 additional restriction sites are provided.

42. The nucleic acid molecule of claim 24 wherein at least 25 additional restriction sites are provided.

43. The nucleic acid molecule of claim 24 wherein at least 30 additional restriction sites are provided.

44. The nucleic acid molecule of claim 24 wherein the *p53* mutation found in a human cancer is selected from the group consisting of: Lys132Arg; Cys135Tyr; Cys141Tyr; Pro151Ser; Gly154Val; Val157Phe; Arg158His; Arg158Leu; Ala161Thr; Tyr163Cys; Val173Leu; Val173Met; Arg175His; Cys176Phe; Cys176Tyr; His179Arg; His179Tyr; Ile195Thr; Tyr205Cys; His214Arg; Tyr220Cys; Tyr234Cys; Met237Ile; Cys238Tyr; Ser241Phe; Cys242Phe; Gly245Asp; Gly245Cys; Gly245Ser; Gly245Val; Arg248Gln; Arg248Leu; Arg248Trp; Arg249Met; Arg249Ser; Gly266Arg; Gly266Glu; Val272Met; Arg273Cys; Arg273His; Arg273Leu; Cys275Tyr; Pro278Leu; Pro278Ser; Arg280Lys; Arg280Thr; Asp281Glu; Arg282Trp; Glu285Lys; and Glu286Lys.

45. The nucleic acid molecule of claim 24 which has a nucleotide sequence as shown in a sequence listing selected from SEQ ID NO: 4-53.

46. A non-naturally occurring nucleic acid molecule which employs a plurality of alternative codons to those present in naturally occurring wild-type human *p53* coding sequence, said alternative codons causing no amino acid changes from wild-type human *p53*, wherein at least a portion of said alternative codons provide additional unique restriction sites to the human *p53* coding sequence, said nucleic acid further comprising a mutation in a codon for a

residue which is post-translationally modified in wild-type p53, said mutation preventing post translational modification of said residue.

47. The nucleic acid molecule of claim 46 wherein the posttranslational modification is phosphorylation.

48. The nucleic acid molecule of claim 46 wherein the posttranslational modification is acetylation.

49. The nucleic acid molecule of claim 46 wherein the posttranslational modification is sumoylation.

50. The nucleic acid molecule of claim 46 wherein the posttranslational modification is ubiquitylation.

51. The nucleic acid molecule of claim 46 wherein the residue which is post-translationally modified in wild-type p53 is selected from the group consisting of: Ser6, Ser9, Ser15, Ser20, Ser33, Ser37, Ser46, Ser315, Ser371, Ser376, Ser378, Ser392, Thr18, Thr81, Lys320, Lys370, Lys372, Lys373, Lys381, Lys382, and Lys386.